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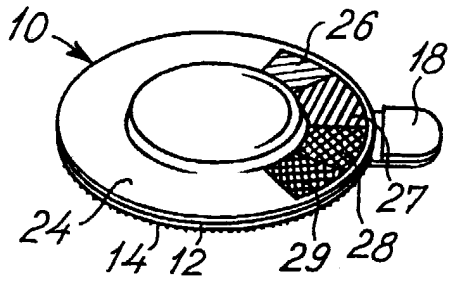

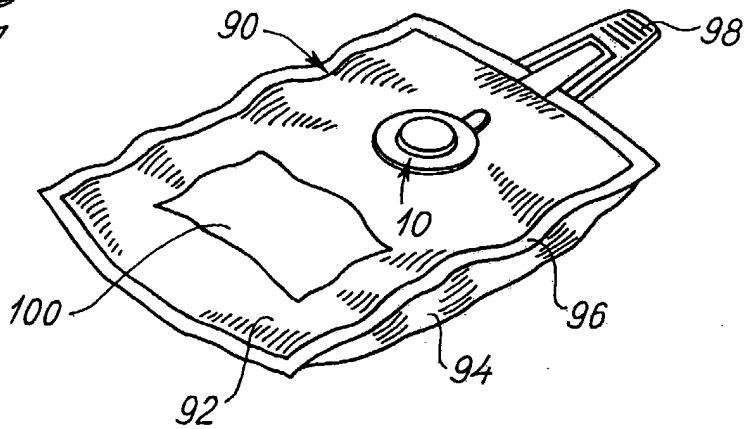

(57) Abstract

The biological activity within a container or bag containing a foodstuff or a human thrombocyte concentrate is monitored by means of an apparatus (10) for indicating the partial pressure of carbon dioxide. The apparatus (10) comprises a first foil (24) of a light-transparent material substantially impermeable to gas and water, a second foil (20) constituting a CO_2-permeable membrane, and an indicator system contained within a sponge (22) which is enclosed within a chamber defined between the first and second foils (24 and 20, respectively). As CO_2 permeates into the chamber defined between the first and the second foils (24 and 20, respectively), the indicator system generates a visible indication in response to exposure to CO, which indication is visible through the first foil (24).

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An Apparatus for Indicating the Presence of CO_2 and a Method of Measuring and Indicating Bacterial Activity within a Container or Bag.

The present invention relates to the technique of measuring and indicating bacterial activity within containers or bags, such as containers or bags containing biological material or samples, such as blood samples, urine samples, blood products, blood fractionation products, infusion fluids, such as enteral or parenteral infusion fluids or nutrients, or biologically degradable materials, or foodstuff.

The present invention more precisely relates to a novel technique of measuring and indicating bacterial activity within containers or bags by measuring and indicating the content of CO_2 within the container or bag in question or permeating from the container or bag in question, which CO_2 is generated by bacterial activity within the container or bag.

The present invention consequently relates to the technique of measuring and indicating the partial pressure of carbon dioxide.

A particular technical field within which the novel technique according to the present invention is particularly applicable is within the field of handling and storing blood samples or products made thereof and blood products or blood fractionation products, such as thrombocyte concentrates or red blood cell concentrates produced in blood banks.

Thrombocyte concentrates are routinely produced in blood banks from freshly donated blood, by well-known separation procedures. The thrombocyte concentrates can be used for the treatment of patients for up to five days from the date of production, during which period they are stored in sterile containers or bags made from a semi-permeable material that allows passage of oxygen (O_2) and carbon dioxide (CO_2). The cells in the thrombocyte concentrate sustain their life exactly the same way as cells within the human body, through a metabolic process, consuming O_2 and producing CO_2. As thrombocyte concentrates are used for infusion into the blood stream of certain patients, maintenance of the sterility of the thrombocyte concentrate during storage is essential to the patients. Thrombocyte concentrates, or e.g. red blood cell concentrates, infected by bacteria or other microorganisms may cause severe complica-

tions such as bacteremia, sepsis, and shock. An infection of the thrombocyte concentrate by bacteria or other microorganisms accidentally introduced during the production or handling of the thrombocytes, or from contaminated bags, tubes, etc., will cause an increase of the metabolic generation of CO_2. Furthermore, it has been realized that an infection may give no other detectable sign than an increase of the production of CO_2, and infected thrombocyte concentrates may thus accidentally be used for patient treatment.

Hitherto, the quality control of thrombocyte concentrates has been done by the blood banks by spot testing: A number of samples are tested, to represent the quality of the total number of thrombocyte units produced. The number of thrombocyte units that are accidentally infected is presumably very low, compared to the total number of units produced; the probability of identifying an infected thrombocyte unit by spot testing is thus very low.

An object of the present invention is to provide a novel technique rendering it possible to carry out a non-invasive measurement and indication of any bacterial activity within containers or bags containing biological material or samples, such as blood samples, urine samples, blood products, blood fractionation products, infusion fluids, such as enteral or parenteral infusion fluids or nutrients, or biologically degradable materials, or foodstuff, in particular containers or bags containing thrombocyte concentrates.

A particular advantage of the present invention relates to the fact that the novel technique according to the present invention renders it possible to monitor and measure biological activity of bacteria or other microorganisms, such as aerobe and anaerobe bacteria within containers or bags which may be hermetically sealed containers or bags, or containers or bags made from permeable or semi-permeable materials allowing the exchange of oxygen and carbon dioxide from the interior of the container or bag in question and the environment.

A further particular advantage of the present invention relates to the fact that the monitoring and measuring of biological activity of bacteria or other microorganisms in accordance with the present invention is

of a quantitative or at least semi-quantitative nature, and not only of a qualitative nature.

A particular feature of the present invention relates to the applicability of the novel technique according to the present invention, as the novel technique renders it possible to provide a low cost indicator apparatus or device which provides a highly accurate measurement and indication, and which may be used within numerous technical fields, such as within the technical field of monitoring patients or persons by transcutaneously measuring the partial pressure of carbon dioxide, and of providing a visual indication of containers or bags containing foodstuff providing an accurate and reliable indication to the customer regarding the freshness of the foodstuff contained within the container in question.

The above object, advantage and feature, and numerous other objects, advantages, and features which will be obvious to a person having ordinary skill in the art and which will be evident from the below detailed description of preferred embodiments implemented in accordance with the teaching of the present invention are in accordance with a first aspect of the present invention obtained by means of an apparatus for indicating the partial pressure of carbon dioxide, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil.

In the present context, the term "substantially impermeable" defines in relation to the term "gas-permeable" that the substantially impermeable material exhibits barrier properties as the permeability of the substantially impermeable material is a factor at least 10 smaller than the permeability of the gas-permeable material, such as a factor 10-100 or more.

Basically, the apparatus according to the first aspect of the present invention constitutes a CO_2 indicator which contains an indicator system generating a visible indication in response to exposure to CO_2. The second foil of the apparatus serves the purpose of providing a CO_2-permeable membrane which is preferably impermeable to water and consequently to a substantial extent blocks the transmission of water through the CO_2-permeable membrane, and through which CO_2 may permeate into contact with the indicator system and further serves the purpose of defining an inner chamber enclosing the indicator system with the first foil, which first foil serves the dual purpose of preventing CO_2 and any other gases or water from permeating into contact with the indicator system from the environment, and consequently of preventing constituents different from carbon dioxide from permeating into contact with the indicator system through a transmission path different from the CO_2-permeable second foil, and of providing a window through which the indicator system may be monitored and through which any indication generated by the indicator system in response to exposure to CO_2 may be monitored.

An example of an impermeable material is a composite foil comprising a 25 µm thick nylon foil and a 60 µm thick polyethylene foil, which foil exhibits a transmission to CO_2 of the order of 16.0 $cm^3/m^2/24$ h at a temperature of 25°C and a relative humidity of 75%, and a transmission to water vapour of the order of 9.2 $g/m^2/24$ h at a temperature of 40°C and a relative humidity of 90%. Similarly, a CO_2-permeable material is a polyethylene foil of a thickness of 95 µm exhibiting a permeability or transmission to CO_2 of the order of 11600 $cm^3/m^2/24$ h at a temperature of 25°C and a relative humidity of 75%, and a transmission to water vapour of the order of 4.4 $g/m^2/24$ h at a temperature of 40°C and a relative humidity of 90%. This PE-foil is a CO_2-permeable, yet water-impermeable foil or material. Preferably, the permeability of the first foil is approx. 100-1000 times less than the permeability of the second foil to CO_2. Furthermore, a foil or material exhibiting a transmission or permeability to CO_2 of the order of 2500 $cm^3/m^2/24$ h at a temperature of 25°C and a relative humidity of 75% is considered a fairly permeable foil or material, whereas a foil or material exhibiting a permeability of transmission of the order of 150 $cm^3/m^2/24$ h at a temperature of 25°C and a relative humidity of 75% is considered a fairly impermeable foil

or material.

The indicator system of the apparatus may be implemented in accordance with any appropriate technique, however, preferably comprises an aqueous solution of a pH-sensitive indicator material generating a visible indication in response to a change of pH. Alternatively, the indicator system may comprise a glycerine-based solution of a pH-sensitive indicator material. The indicator material may e.g. be dibromthymolsulfonphthalein, also known as Bromethymol Blue, and the aqueous solution may preferably comprise a buffer, such as $NaHCO_3$. The pH-sensitive indicator material and the buffer are preferably selected so as to create a pH indicator system in which a state of equilibrium is created corresponding to the normal partial pressure of CO_2 and so as to create an indicator system in which a change of the pCO_2 from a normal state to an abnormal state results in the generation of a clearly visual indication of the pH-sensitive indicator material.

Provided a thrombocyte concentrate is monitored by means of the apparatus according to the first aspect of the present invention, the equilibrium partial pressure of carbon dioxide corresponding to the normal metabolic generation of CO_2 by the thrombocytes is of the order of 20-30 mmHg. Provided the partial pressure of CO_2 increases, a threshold is exceeded, resulting in the generation of a visual indication by the indicator system and consequently by the pH-sensitive indicator material. For most biological materials or substances, e.g. blood products or blood fraction products, the indicator system is preferably provided as a mirror image of a biological liquid in which indicator system a pH of the order of approx. 7.00-7.40 and a concentration of bicarbonate ions of the order of 5-25 mM/l, substantially corresponding to the pH and the concentration of bicarbonate ions, respectively, of biological liquids. It is believed that a more accurate and precise indicator system is provided by providing an indicator system constituting a mirror image of the material or substance to be monitored, as secondary reactions or substitutions are eliminated from influencing the relevant chemical reaction of the indicator system. Generally speaking, however, the indicator system has to be adjusted to react, causing a visible indication at a specific pCO_2 level. Thus, for alternative applications, the indication system is to be optimized to provide a specific colour change at

the relevant level of pCO_2.

Various alternative and relevant indicator materials are dichlorosulfonphthalein or phenolsulfonphthalein or other acid or base indicators, e.g. those indicators which are listed in Ullmanns "Encyklopädie der technischen Chemie", Verlag Chemie, Vol. 13, 4th Edition, p. 185. Further preferably, the aqueous solution comprises NaCl for providing a mirror image of the biological liquid as discussed above, and in the aqueous solution, the pH depends on the pCO_2 according to the following equation:

$$pH = K - \log pCO_2, \text{ where}$$

K is a constant, provided that the concentration of $NaHCO_3$ is between 10^{-3}M and 10^{-1}M. The chemical balance is adjusted by the provision of the buffer, and is, provided thrombocyte concentrates are to be monitored, adjusted in such a way that the indication being Bromethymol Blue is blue at low and normal pCO_2 values (0 - 30 mmHg) and provides a colour change from blue to green and further to yellow at higher pCO_2 values.

According to a particular embodiment of the apparatus according to the present invention, the apparatus further comprises a sponge of an absorbing material, which sponge is concealed within the inner chamber defined within the apparatus, and the indicator system is soaked in the sponge.

In order to render it possible to fixate the apparatus according to the present invention to a container or bag, such as a container or bag containing a thrombocyte concentrate, the apparatus according to the first aspect of the present invention preferably further comprises a support foil having a through-going aperture, which support foil is circumferentially joined to the inner foil of the apparatus in facial contact therewith through a first side surface of the support foil so as to expose the second foil constituting the CO_2-permeable membrane of the apparatus in the aperture of the support foil. Further preferably, the support foil is provided with an adhesive layer provided at a side surface of the support foil opposite to the first side surface thereof.

In order to render it possible to handle and store the apparatus prior to use, the apparatus may advantageously comprise a release foil covering the adhesive layer and the second foil exposed in the aperture of the support foil in order to prevent that contamination, such as dust, unintentionally adheres to the adhesive layer, and further for preventing that the CO_2-permeable membrane, and consequently the indicator system of the apparatus, is exposed to gases or even CO_2 prior to use, which gases might jam or ruin the operation of the apparatus.

As stated above, the apparatus according to the first aspect of the present invention may comprise a sponge in which the indicator system is soaked. Whether or not the apparatus comprises a sponge, the first foil is preferably shaped with an outwardly protruding dome, below which the inner chamber containing the indicator system and further the sponge, if any, is defined.

In the presently preferred embodiment of the apparatus according to the first aspect of the present invention, the apparatus constitutes a single or stand-alone apparatus which may be easily adhered or fixated to a container within or outside the container in question, optionally by means of the support foil of the apparatus. Alternatively, the apparatus according to the first aspect of the present invention may be integrated into the container or bag, the content of which is to be monitored as the first foil of the apparatus may constitute a wall component of the container or bag in question.

Further alternatively, the apparatus according to the first aspect of the present invention may be integrated into the container or bag, the content of which is to be monitored as the second foil of the apparatus may constitute a wall component of the container or bag in question. Thus, in accordance with alternative embodiments of the apparatus according to the first aspect of the present invention, the first foil, and a second foil, respectively, are constituted by a foil constituting a wall component of the container or bag in question, containing the material or the sample, the bacteriological activity of which is to be monitored by means of the apparatus.

In accordance with the concept of integrating the apparatus according to

the first aspect of the present invention into the container or bag containing the material or the sample, the bacteriological activity of which is to be monitored by means of the apparatus, the indicator system may advantageously be contained within an adhesive layer through which the apparatus is adhered to the foil constituting a wall component of the container or bag, i.e. adhered to the inner surface of the foil constituting the wall component of the container or bag, provided the foil constitutes the first foil of the apparatus according to the first aspect of the present invention, and adhered to the outer surface of the foil constituting the wall component of the container or bag, provided the foil constitutes the second foil of the apparatus according to the first aspect of the present invention, respectively.

In accordance with the presently preferred embodiment of the apparatus according to the first aspect of the present invention, the first foil is a multi-layer film comprising at least one layer of nylon and at least one layer of polyethylene, the second foil is a polyethylene foil or alternatively a silicone rubber foil, the support foil is a PVC foil, and the sponge, if any, is preferably made of a filter paper material, or alternatively made from woven material or mesh material. Alternatively, the first foil may comprise a polyester foil, and the second foil may comprise a silicone foil.

As stated above, the apparatus according to the first aspect of the present invention is advantageously applied to or within containers or bags containing biological material or samples, such as blood samples, urine samples, blood products, blood fractionation products, infusion fluids, such as enteral or parenteral infusion fluids or nutrients, or biologically degradable materials. Alternatively, the apparatus according to the first aspect of the present invention may be used for transcutaneously monitoring the partial pressure of carbon dioxide of a patient or person, such as a prematurely born infant. Furthermore, as stated above, the apparatus according to the first aspect of the present invention may be used within the foodstuff industry, providing a low cost, yet reliable and precise indicator, rendering it possible to provide an objective indication to the customers regarding the freshness of the foodstuff contained within a foodstuff container, such as a plastic container containing meat, or a meat container or tray wrapped into a

plastic foil.

According to a second aspect of the present invention, an apparatus is provided which may be integrated into or enclosed within a sealed container, which container may be made from a permeable or impermeable material, dependent on the application. The apparatus for indicating the partial pressure of CO_2 according to the second aspect of the present invention comprises:

a foil of a light-transparent, CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2, said foil being folded and sealed so as to define a sealed inner chamber, and said indicator system being enclosed within said inner chamber and being visible through said light-transparent foil.

According to the preferred embodiment of the apparatus according to the second aspect of the present invention, the foil defines a tubular segment sealed at opposite ends thereof. Like the above described apparatus according to the first aspect of the present invention, the apparatus according to the second aspect of the present invention may be implemented according to the above embodiments and comprising the above features.

According to the first and second aspects of the present invention, apparatuses are provided for indicating the partial pressure of carbon dioxide, in particular apparatuses for measuring and indicating the partial pressure of carbon dioxide generated by biological activity within containers or bags containing biological material or samples, such as blood samples, urine samples, blood products, blood fractionation products, infusion fluids, such as enteral or parenteral infusion fluids or nutrients, or biologically degradable materials, or foodstuff. The apparatuses according to the present invention provide semi-quantitative information, apart from a quality information, e.g. a quality information regarding the freshness of foodstuff contained within a container or bag. Furthermore, the biological material or sample contained within a container or sample may be monitored without providing access to the content of the container or bag in question, i.e. to the biological material or sample, and consequently without compromising the sterility of

the material or sample.

According to a third aspect of the present invention, a method of measuring and indicating bacterial activity within a container or bag of a gas-permeable material containing a biological material or sample, such as a blood sample, a urine sample, a blood product, a blood fractionation product, e.g. a thrombocyte concentrate, an infusion fluid, such as an enteral or parenteral infusion fluid or nutrient, or a biologically degradable material, or a foodstuff, is provided, which method comprises the steps of:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil, and

b) arranging said apparatus in facial contact with said wall of said container or bag so as to arrange said second foil in gas-communicating relationship with said wall and said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said wall and through said second foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag.

According to a fourth aspect of the present invention, a method of measuring and indicating bacterial activity within a container or bag of a gas-impermeable material containing a biological material or sample, such as a blood sample, a urine sample, a blood product, a blood fractionation product, e.g. a thrombocyte concentrate, an infusion fluid, such as an enteral or parenteral infusion fluid or nutrient, or a biologically degradable material, or a foodstuff, is provided, which method comprises the following steps:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil, and

b) arranging said apparatus within said container or bag so as to arrange said second foil in gas-communicating relationship with said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said second foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag, and so as to expose said first foil through a light-transparent section or wall of said container or bag.

According to a fifth aspect of the present invention, a method of measuring and indicating bacterial activity within a container or bag of a gas-impermeable material containing a biological material or sample, such as a blood sample, a urine sample, a blood product, a blood fractionation product, e.g. a thrombocyte concentrate, an infusion fluid, such as an enteral or parenteral infusion fluid or nutrient, or a biologically degradable material, or a foodstuff, is provided, which method comprises the steps of:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water, constituting at least a wall section of said container or bag,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator

system being enclosed within said inner chamber and being visible through said first foil, and

b) arranging said apparatus so as to arrange said first foil constituting said wall section of said container or bag and so as to arrange said second foil in gas-communicating relationship with said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said second foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag.

According to a sixth aspect of the present invention, a method of measuring and indicating bacterial activity within a container or bag of a gas-impermeable material containing a biological material or sample, such as a blood sample, a urine sample, a blood product, a blood fractionation product, e.g. a thrombocyte concentrate, an infusion fluid, such as an enteral or parenteral infusion fluid or nutrient, or a biologically degradable material, or a foodstuff, is provided, which method comprises the following steps:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a foil of a light-transparent, CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2, said foil being folded and sealed so as to define a sealed inner chamber, and said indicator system being enclosed within said inner chamber and being visible through said light-transparent foil, and

b) arranging said apparatus so as to arrange said foil in gas-communicating relationship with said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag, and so as to expose said foil through a light-transparent section or wall of said container or bag.

The methods according to the third, fourth, fifth, and sixth aspect of the present invention constitute novel measuring and indicating tech-

niques according to which the apparatuses according to the first and second aspects of the present invention are employed.

Within the literature, various measuring techniques and measuring devices of somewhat different structure and fulfilling different purposes are described. Thus, US Patent No. 4,732,156 describes a transdermal dosimeter, and US Patent No. 4,821,733 describes a transdermal detection system for detecting ethanol or glucose. Reference is made to these US patents, and both US patents are herewith incorporated in the present specification by reference. A transdermal dosimeter structure is disclosed in International Patent Application, International Publication No. WO 87/00744. International Patent Application, International Publication No. WO 89/04630, also describes a transdermal vapour collection method and apparatus. International Patent Application, International Publication No. WO 90/02511, European Patent Application, Publication No. 0 083 941 and European Patent Application, Publication No. 0 143 550, describe various measuring and indicator techniques. A carbon dioxide indicator is known from International Patent Application, International Publication No. WO 90/01695, to which reference is made.

The technique of transcutaneously measuring the partial pressure of a blood gas constituent, such as the partial pressure of carbon dioxide, is extensively described in the literature, e.g. in numerous patents, such as Danish Patent No. 143.246 and Danish Patent No. 139.895. Furthermore, it is known to use CO_2-monitors or indicators for respiration monitoring, vide e.g. US Patent No. 4,728,499, to which reference is made and which is hereby incorporated in the present specification by reference.

Within the container and packaging industry, various techniques for indicating the sterility or the lack of sterility of a sealed container are known, e.g. from French Patent No. 2 461 662, US Patent No. 4,049,121, GB Patent Application No. 2 208 287, German Published Patent Application No. DE OS 39 19 405 and Japanese Patent Application, Appln. No. 62-206290, published under Publication No. 1-58670, to which patent specifications reference is made, and which above-mentioned US patent is hereby incorporated in the present specification by reference.

The present invention will now be further described with reference to the drawings, in which

Fig. 1 is an exploded, perspective view of a first, presently preferred embodiment of a pCO_2 indicator implemented in accordance with the teaching of the present invention,

Fig. 2 is a perspective view of the assembled first embodiment of the pCO_2 indicator implemented in accordance with the teaching of the present invention, further including reference indicator codings,

Fig. 3 is a perspective view of a strip carrying or supporting two pCO_2 indicators according to the first embodiment of the present invention also shown in Fig. 1, illustrating the technique of assembling the pCO_2 indicators in a production plant,

Fig. 4 is a vertical sectional view of a second, slightly modified embodiment of the pCO_2 indicator as compared to the first embodiment shown in Figs. 1-3, arranged on a skin surface part of a patient or person for transcutaneously indicating the partial pressure of CO_2 of the patient or person,

Fig. 5 is a perspective view of an assembly of a third embodiment of the pCO_2 indicator implemented in accordance with the teaching of the present invention, and a bio-electric signal-sensing electrode, i.e. an electrode for sensing a bio-electric signal, such as the ECG, the EEG, the heart rate or the like of a patient or person,

Fig. 6 is a perspective view of a presently preferred application of the first embodiment of the pCO_2 indicator shown in Figs. 1-3, within the field of monitoring live human thrombocytes enclosed within a container or bag,

Fig. 7 is a perspective view of an alternative application of the first embodiment of the pCO_2 indicator shown in Figs. 1-3, within the field of monitoring biological samples or fluids, such as blood samples, urine samples, blood products, blood fractionation products, infusion fluids, such as enteral or parenteral infusion fluids or nutrients, or biologic-

ally degradable materials, or foodstuff, growth substrates, etc., or alternatively within the technical field of monitoring foodstuff,

Fig. 8 is a perspective view of a further alternative application of the pCO_2 indicator according to the present invention, illustrating a sample-containing bottle comprising a sealed cap in which a further alternative embodiment of the pCO_2 indicator implemented in accordance with the teaching of the present invention is integrated,

Figs. 9 and 10 are perspective views of further alternative applications of the pCO_2 indicator technique according to the present invention within the field of monitoring foodstuff, such as meat contained within a tray-shaped container, by means of two alternative embodiments of the pCO_2 indicator implemented in accordance with the teaching of the present invention,

Figs. 11 and 12 are exploded, perspective views similar to the view of Fig. 1 of still further alternative embodiments of the pCO_2 indicator implemented in accordance with the teaching of the present invention, and

Figs. 13 and 14 are perspective views similar to the views of Figs. 6 and 10, respectively, of the application of the alternative embodiment of the pCO_2 indicator shown in Figs. 11 and 12, respectively.

In Figs. 1 and 2, a first, presently preferred embodiment of a pCO_2 indicator is shown, implemented in accordance with the teaching of the present invention. The first embodiment is designated the reference numeral 10 in its entirety and comprises an annular support foil 12 in which a central circular aperture is defined and which is provided with adhesive coatings 14 and 16 on opposite side surfaces thereof. The annular support foil 12 is provided with an outwardly protruding flap which is also provided with the adhesive coating 16 and covered by a flap component, designated the reference numeral 18 in order to render it possible to grasp the pCO_2 indicator.

The pCO_2 indicator further comprises a circular CO_2-permeable, yet water-impermeable membrane 20 which defines an outer diameter larger

than the inner diameter of the through-going aperture of the support foil 12. The CO_2-permeable membrane 20 is arranged in contact with the adhesive coating 16 of the support foil 12 covering the through-going circular aperture of the support foil 12.

On top of the CO_2-permeable membrane 20, a sponge 22 is arranged which sponge comprises an indicator system, e.g. a pH indicator which generates a visible indication when exposed to carbon dioxide, in accordance with the shift of the equilibrium of the equation:

$$H_2O + CO_2 \rightleftarrows H^+ + HCO_3^-$$

Examples of indicator systems or compounds are listed below.

The sponge 22 and further an exposed annular rim part of the CO_2-permeable membrane 20, which rim part is not covered by the sponge 22, and also the uncovered main part of the adhesive coating 16 of the support foil 12 is covered by a light-transparent, yet gas- and water-impermeable cover foil 24 which is provided with a central, upwardly protruding dome, below which the sponge 22 and the pCO_2 indicator system or compound is enclosed. It is to be realized that the sponge 22 may be omitted, as the dome of the cover foil 24 may in itself define a chamber above the CO_2-permeable membrane 20, in which chamber the CO_2 indicator system is enclosed.

The adhesive coating 14 exposed at the lower or outer side surface of the support foil 12 is preferably a water-based adhesive or glue which is compatible with the material, such as the skin surface of a patient or person, or a container or bag made from a plastic material with which the pCO_2 indicator is to be brought into contact. The adhesive coating 16 may also be made from a water-based glue, provided the cover foil 24 is welded to the CO_2-permeable membrane 20 which is further preferably welded to the support foil 12 defining a sealed chamber below the dome of the cover foil 24 and above the CO_2-permeable membrane 20, which chamber communicates with the environment through the CO_2-permeable membrane exclusively due to the circumferential weld and further the impermeable properties of the cover foil 24. In a slightly modified embodiment, the CO_2-permeable membrane 20 and the support foil 12 are integra-

ted into a single component.

In Fig. 2, the pCO_2 indicator 10 is shown in the assembled state, ready for use, and further provided with colour codings 26, 27, 28, and 29, which colour codings are printed on an exposed circumferential rim part of the cover foil 24 adjacent to the dome of the cover foil 24. The colour codings 26-29 represent reference markings or indications with which the CO_2 indicator system visible through the light-transparent cover foil 24 may be compared for determining a specific partial pressure of carbon dioxide corresponding to a specific colour coding, i.e. one of the colour codings 26-29, of the material, patient, person, or sample, to which the pCO_2 indicator is applied or arranged.

In Fig. 3, two pCO_2 indicators of the above described structure, i.e. implemented in accordance with the first embodiment described above, are shown designated the reference numerals 10' and 10'', respectively, applied to a release foil 80.

The pCO_2 indicator 10 is preferably produced in an automatic production apparatus in which a length of the support foil material is provided with adhesive coatings on opposite side surfaces and cut into the annular configuration shown in Fig. 1, also defining the flap to which the flap component 18 is applied. The flap component 18 may constitute a segment of a strip covering the length from which the annular support foil 12 is cut.

Similarly, the pCO_2-permeable membrane 20 is cut from a continuous length of the pCO_2-permeable membrane material. The sponge 22 and the cover foil 24 are also cut from continuous lengths of those materials, whereupon the sponge 22 is soaked with the pCO_2 indicator system. The support foil 12 having the adhesive coatings applied to opposite side surfaces thereof, the CO_2-permeable membrane 20, the sponge 22, and the cover foil 24 are arranged in registration and assembled optionally omitting the sponge 22, and preferably providing a sealing by providing a circumferential weld seam, welding the support foil 12, the CO_2-permeable membrane 20 and the cover foil 24 together.

After or at the stage of assembling the pCO_2 indicator 10, the indicator

is applied to the release foil 80, as shown in Fig. 3, which release foil 80 serves the purpose of protecting the adhesive coating 14 which is exposed at the lower side surface of the support foil 12 from unintentionally adhering to materials or substances and from being contaminated by particles, dust, etc.

In Fig. 4, a second, or slightly modified embodiment of the pCO_2 indicator is shown, designated the reference numeral 40. The second embodiment of the pCO_2 indicator implemented in accordance with the teaching of the present invention basically a support foil 42 of an annular configuration defining a central, circular aperture. The support foil 42 basically corresponds to the support foil 12 described above and is provided with adhesive coatings 44 and 46 corresponding to the adhesive coatings 14 and 16 described above. The pCO_2 indicator 40 further comprises a CO_2-permeable membrane 50 and a sponge 52 corresponding to the membrane 20 and the sponge 22, respectively, described above. Similar to the pCO_2 indicator 10 described above, the pCO_2 indicator 40 is provided with a cover foil designated the reference numeral 54. As is evident from Fig. 4, the cover foil 54, the CO_2-permeable membrane 50 and the support foil 42 are welded together along a circular or circumferential weld seam designated the reference numeral 48.

The pCO_2 indicator 40 shown in Fig. 4 is adapted to be used for monitoring the partial pressure or carbon dioxide of a patient or person, such as a prematurely born child, a skin surface section of which is shown in Fig. 4 designated the reference numeral 30. The skin surface section 30 comprises three sections, viz. a hypodermic section or layer 32, an epidermic section or layer 34, and a dermic section or layer 36. As is evident from Fig. 4, a chamber 56 is defined above the layer 36 adjacent to the lower side surface of the CO_2-permeable membrane 50. The chamber 56 may be filled by a contact liquid, such as a CO_2 transfer liquid.

In Fig. 5, an assembly 60 is shown, which assembly is assembled from a bio-electric signal-sensing electrode and a pCO_2 indicator implemented in accordance with the teaching of the present invention. The pCO_2 indicator is designated the reference numeral 66 in its entirety and is arranged within a circular aperture of an electrically conductive plate 62

which may be made from a metal, such as a noble metal, or from carbon fibre material. A lower side surface of the plate 62 is provided with an electrically conductive glue 64, and the upper side surface of the plate 62 is covered by a CO_2-permeable foil 68 which constitutes a component of the pCO_2 indicator 66 similar to the cover foils 24 and 54 described above with reference to Figs. 1 and 4, respectively. A conductor 70 is connected in electrically conductive connection with the electrically conductive plate 62 through a rivet or soldering connection 72.

Whereas the second and third embodiments of the pCO_2 indicator according to the present invention discussed above with reference to Figs. 4 and 5 are preferably used for monitoring or measuring the partial pressure of a person or patient, the above described first, and presently preferred embodiment of the pCO_2 indicator according to the present invention is adapted to be used for detecting bacteriological activity of biological samples or systems, such as blood or urine samples, e.g. live human thrombocytes. Thus, in Fig. 6, the pCO_2 indicator 10 is applied to an outer side surface of a container or bag 90 containing live human thrombocytes. The bag 90 is composed of two oxygen and carbon dioxide permeable foils 92 and 94 which are welded together along a circumferential weld 96, together constituting the bag 90 and also integrally connected to an eyelet 98 by means of which the bag 90 may be hung on a wire, or hook or similar suspension means. The bag 90 is further provided with an outer label 100 on which information is printed or written, identifying the thrombocyte content of the bag 90 and the relevant data thereof, such as the date of production of the human thrombocyte sample and of the maximum period of time of storing of the sample. In case the live human thrombocytes are exposed to bacteriological activity, carbon dioxide is generated by the bacteria, which carbon dioxide is easily detected by means of the pCO_2 indicator 10, as the carbon dioxide permeates through the foil or membrane 92 of the bag 90 and into the indicator 10.

In Fig. 7, a similar application of the pCO_2 indicator is shown, in accordance with which application the above described first, presently preferred embodiment of the pCO_2 indicator 10 is arranged on a container 110, which container is composed of a cover part 112 and a bottom part 114. The cover part 112 and the bottom part 114 may be welded together along a circumferential rim part of the cover part 112 in order to pro-

vide a hermetically sealed container. Provided the cover part 112 of the container 110 is made from a CO_2-permeable material, the pCO_2 indicator 10 may be arranged on the outer side surface of the container 110. In case the cover part 112 of the container 110 is made from a CO_2- impermeable material, the pCO_2 indicator 10 is arranged within the chamber defined within the container 110.

According to the teaching of the present invention, the pCO_2 indicator, such as the pCO_2 indicator designated the reference numeral 10 shown in Figs. 6 and 7, may be integrated into the container or bag which contains a sample or system which is to be monitored by means of the pCO_2 indicator. Thus, the cover foil of the pCO_2 indicator, such as the cover foil 24 shown in Figs. 1 and 2, may constitute a wall component of the container or bag which contains the sample or system which is to be monitored. Reference is made to the description below referring to the embodiment shown in Fig. 9 which illustrates the technique of integrating the pCO_2 indicator into a wall component of the container or bag.

In Fig. 8, an alternative application of the teaching of the indicator technique according to the present invention is shown. Thus, in Fig. 8, a bottle 150 containing a biological substrate or material, e.g. a growth medium or substrate, is shown. The bottle 150 is sealed by means of a closure 152 which is provided with an integral pCO_2 indicator 154 implemented in accordance with the teaching of the present invention. Thus, provided the biological material or substance contained within the bottle 150 generates carbon dioxide, e.g. due to bacteriological growth within the bottle 150, the pCO_2 indicator 154 indicates an increase of the partial pressure of carbon dioxide generated within the hermetically sealed bottle 150.

In Figs. 9 and 10, a further alternative application of the pCO_2 indicator technique according to the present invention is illustrated. In Figs. 9 and 10, a container 120 is shown comprising a tray-shaped support component 122, e.g. a plastic or cardboard tray component. Within the tray 122, chopped meat 124 is contained and covered by means of a light-transparent, oxygen and carbon dioxide impermeable foil 126. A label 128 is applied to the outer side surface of the foil 126. In order to inform the customer about the quality of the content of the container

120, i.e. the quality of the chopped meat, pCO_2 indicators implemented in accordance with the teaching of the present invention are provided.

In Fig. 9, two pCO_2 indicators are integrated into the foil 126, one of which pCO_2 indicators is designated the reference numeral 130 in its entirety. The pCO_2 indicator 130 basically comprises a tray-shaped component 132 of a CO_2-permeable material, which component 132 is welded to the foil 126 along a rim part 134. Within the rim part 134, a pCO_2 indicator system 136 is enclosed, which indicator system may inform the customer about any bacteriological activity within the chopped meat 124 giving origin to an increase of the partial pressure of carbon dioxide within the container 120 and consequently within the indicator system contained within the carbon dioxide permeable tray 132.

In Fig. 10, an alternative embodiment of the pCO_2 indicator is shown designated the reference numeral 140 in its entirety. The pCO_2 indicator 140 basically comprises a tubular segment of a CO_2-permeable plastic material, within which tubular segment a pCO_2 indicator compound 144 is enclosed. The tubular segment 142 is cut from a continuous length of a tube containing the pCO_2 indicator system 144 as the individual tubular segments, such as the tubular segment 142, is sealed by means of constrictions 146.

In accordance with the applications shown in Figs. 9 and 10, the label 148 may be provided with information regarding a specific visual indication of the pCO_2 indicators 130 and 140, which visible indication may correspond to a specific increased bacteriological activity within the chopped meat 124. Thus, the pCO_2 indicators 130 and 140 may inform the customer that a specific chopped meat sample has been exposed to increased bacteriological activity and should consequently not be purchased.

In Fig. 11, a seventh embodiment of the pCO_2 indicator is shown, implemented in accordance with the teaching of the present invention. The seventh embodiment is designated the reference numeral 160 in its entirety and is adapted to be adhered to a gas-permeable foil of a bag or container, the content of which is to be monitored by means of the pCO_2 indicator 160, e.g. as shown in Fig. 13 illustrating the application of

the pCO_2 indicator 160 within the field of monitoring the bacteriological activity within a human thrombocyte sample as described above with reference to Fig. 6.

The seventh embodiment 160 comprises a light-transparent and gas-impermeable plastic foil 162 of a circular configuration which is provided with an annular covering 164 which defines a central window 166 of the foil 162. The foil 162 constitutes a foil similar to the cover foil 24 of the first embodiment 10 described above with reference to Figs. 1-3. The seventh embodiment 160 comprises in accordance with the teaching of the present invention a pH indicator generating a visible indication when exposed to carbon dioxide as discussed above with reference to Fig. 1. The pH indicator is bonded to a support body 168 which may be constituted by a sponge or, alternatively and preferably, be constituted by a glue layer. The support body 168 is adhered to the lower side surface of the foil 162, i.e. the side surface of the foil 162 opposite the annular covering 164. Provided the support body is constituted by a sponge, the sponge is adhered to the foil 162 by means of an adhesive, and provided the support body is constituted by a glue layer, the support body adheres directly to the support foil through the glue or adhesive of the support body.

The reference numeral 172 designates an adhering surface of the support body, which adhering surface may be constituted by an adhesive or glue layer applied to the support body, provided the support body is constituted by a sponge. Alternatively, provided the support body is constituted by a glue layer, the adhering surface is constituted by an exposed surface of the support body 168. For protecting the support body 168 from being contaminated prior to use, a release foil 174 is provided. The support body 168 may comprise the pH indicator in a homogeneous suspension throughout the support body. Alternatively, the pH indicator may be concentrated within the central part of the support body 168, which central part is visible through the window 166 of the foil 162.

The seventh embodiment 160 shown in Fig. 11 is highly advantageous from a production point of view as the embodiment is easily produced from a first continuous web of the foil material from which the foil 162 is produced. The first web is sandwiched between a second continuous web

which is provided with apertures defining the windows of the individual pCO_2 indicators from which second web the covering 164 is produced and a glue layer from which the support body 168 is produced integrally comprising the pH indicator. The glue layer is covered by a third continuous web of the release foil material from which the release foil 174 is produced. After the production of the sandwich comprising the three continuous webs and the adhesive layer, the circular pCO_2 indicators are cut or punched from the sandwich.

The seventh embodiment 160 of the pCO_2 indicator implemented in accordance with the teaching of the present invention may be used for monitoring bacteriological activity within e.g. a bag containing human thrombocytes, such as the bag 90 shown in Fig. 13, or alternatively be used for monitoring bacteriological activity within a bag or a container in which a sample or foodstuff product is enclosed within a foil of a gas-permeable material. It is to be realized that the seventh embodiment 160 of the pCO_2 indicator shown in Fig. 11 differs from the above described embodiments in that the indicator employs the gas-permeable foil of the bag or container in which a material or a sample is contained and the bacteriological activity in which is to be monitored. Thus, the embodiment 160 may alternatively be used in connection with e.g. containers or bags similar to the containers or bags shown in Figs. 7-10.

In Fig. 12, an eighth embodiment of the pCO_2 indicator is shown implemented in accordance with the teaching of the present invention. The eighth embodiment is designated the reference numeral 180 in its entirety. The eighth embodiment 180 of the pCO_2 indicator comprises a foil 182 of a gas-permeable material, which foil constitutes a foil similar to the CO_2-permeable membrane 20 of the first embodiment 10 of the pCO_2 indicator described above with reference to Figs. 1-3. The eighth embodiment 180 further comprises a support body 184 similar to the support body 168 of the seventh embodiment 160 described above with reference to Fig. 11. The support body 184, thus, may be constituted by a sponge or, alternatively and preferably, be constituted by a glue layer. Within a central area 186 of the support body 184, the pH indicator of the pCO_2 indicator is provided.

The pH indicator of the central area 186 may be constituted by any ap-

propriate pH indicator system, such as the systems described below in the examples. The pH indicator may alternatively be provided as a homogeneous suspension of the adhesive layer 184, in which instance, however, the pH indicator may be brought into contact with a biological material, such as a foodstuff which for toxic reasons may be non-avantageous. Therefore, the pH indicator is preferably provided within the central area 186 of the support body 184, exclusively. The support body 184 is at its lower side surface adhered to the gas-permeable foil 182 and provides an exposed adhering surface 188 which may be constituted by the adhesive material of the support body 184 itself. Alternatively, in case the support body 184 is constituted by a sponge, a glue layer may be provided defining the adhering surface 188. In case a separate glue layer or adhsive is provided, constituting the adhering surface 188, the adhesive may be constituted by a non-light-transparent adhesive defining a central window similar to the window 166 shown in Fig. 11, which window is provided in registration with the central area 186 of the support body 184 for providing a window through which the pH indicator of the central area 186 is visible. A release foil 190 is further provided for protecting the adhering surface 188 of the pCO_2 indicator 180 prior to use. The eighth embodiment 180 of the pCO_2 indicator is, like the above described seventh embodiment 160, advantageously produced from a web assembly sandwiching the glue material from which the support body 184 is produced.

The eighth embodiment 180 may advantageously be used for the same purpose as the above described embodiments 130 and 140, described above with reference to Figs. 9 and 10, viz. the purpose of monitoring any bacteriological activity within a foodstuff, such as chopped meat 124, contained within a container 120. The eighth embodiment 180 is, as is evident from Fig. 14, adhered to the inner side surface of the foil 126 of the container 120. Thus, the intentional application of the eighth embodiment 180 of the pCO_2 indicator differs from the intentional application of the seventh embodiment 160 of the pCO_2 indicator in that the eighth embodiment 180 is to be arranged within the container or bag which is constituted by a gas-impermeable foil, whereas the seventh embodiment 160 is arranged at the outer side surface of the foil of the bag or container, which foil is made from a gas-permeable material.

The seventh embodiment 160 and the eighth embodiment 180 may, apart from the adhesion to the foil of the bag or container, be fixated at the foil through a circumferential weld seam along the outer rim of the embodiment in question, which weld seam seals the foil 162 and the foil 182 of the embodiments 160 and 180, respectively, to the foil of the container or bag.

Example 1

A prototype implementation of the pCO_2 indicator 10 described above with reference to Figs. 1-3 was made from the following components: the support foil 12 was a 145 µm thick PVC foil of an outer diameter of 30 mm and having a through-going aperture of a diameter of 15 mm. The adhesive coating 14 was an acrylic adhesive applied as a coating or layer of a thickness of 50 µm, and the adhesive coating 16 was an acrylic adhesive applied as a coating or layer of a thickness of 50 µm. The pCO_2-permeable membrane 20 was a semi-permeable membrane made from polyethylene of a thickness of 95 µm of an outer diameter of 22 mm. The sponge 22 was omitted. The cover foil 24 was provided with a central dome of a diameter of 18 mm and a height of 0.5 mm. The outer diameter of the cover foil was identical to the outer diameter of the support foil 12 and consequently measured 30 mm. The cover foil 24 was made from a composite multilayer film comprising a single 25 µm thick layer of nylon and a single 60 µm thick layer of polyethylene and had an overall thickness of 85 µm. The indicator system contained within the pCO_2 indicator was 0.15 ml of a saturated aqueous solution of Bromethymol Blue, which aqueous solution contained 150 mM NaCl and 15 mM $NaHCO_3$, constituting a buffer. The release foil was a 75 µm silicone-coated paper foil.

Provided the partial pressure of carbon dioxide was low, the Bromethymol Blue indicator was blue, and as the partial pressure of carbon dioxide shifted beyond 30 mmHg, the indicator system shifted from blue to green, and at higher levels of pCO_2 further to yellow. The prototype implementation was tested in a blood bank and also used for transcutaneously measuring the partial pressure of carbon dioxide of a test person. The prototype implementation responded correctly when exposed to carbon dioxide.

Example 2

Alternative relevant materials are: the membrane of the pCO_2 indicator may be made from any semi-permeable material, such as silicone rubber, polyethylene, polypropylene, polytetrafluorethylene, or combinations thereof, that allows the transmission of CO_2, but excludes transmission of H_2O to any substantial extent in order to guarantee that the pCO_2 on either side of the membrane is the same when the indicator is in a state of equilibrium. In the state of equilibrium, the pCO_2 inside the pCO_2 indicator is identical to the pCO_2 outside the pCO_2 indicator, and consequently within the material or sample contained within the container or bag which is monitored by means of the pCO_2 indicator. A change of pCO_2 within the material or sample gives origin to a change of the pCO_2 outside the pCO_2 indicator, and after a new state of equilibrium has been reached, results in an identical change of pCO_2 within the pCO_2 indicator. The change of pCO_2 within the pCO_2 indicator gives rise to a pH change causing a colour change of the indicator system.

The indicator system may constitute any pH indicator system capable of generating a visible colour change within the relevant pCO_2 and pH range. Examples of relevant indicator systems are listed in the below Table 1 and in Ullmanns "Encyklopädie der technischen Chemie", Verlag Chemie, Vol. 13, 4th Ed., p. 185.

Table 1

pH Indicators

Range of visible colour change	Indicator	Colour Change acidic	alkaline	Indicator Solution (eth. = ethanol, w = water)
0.2-1.8	cresol red	red	yellow	0.1% in eth. (20%)
1.2-2.8	m-cresol purple	red	yellow	0.1% in 0.003 n NaOH
1.2-2.8	thymol blue	red	yellow	0.1% in eth.
2.0-4.4	2.6-dinitrophenol	colour-less	yellow	0.1% in eth. (70%)
2.8-4.7	2.4-dinitrophenol	colour-less	yellow	0.1% in eth. (70%)
2.9-4.0	4-dimethylamino-azobenzene C.I. 11020	red	orange/ yellow	0.1-0.5% in eth. (90%)
3.0-4.6	bromophenol blue	yellow	purple	0.1% in eth. (20%)
3.0-5.2	Congo red	blue/ violet	red/ orange	0.2% in w.
3.1-4.4	methyl orange, C.I.13025	red	yellow/ orange	0.1% in eth.
3.5-5.5	ethoxy chrysoidine, hydrochloride	red	yellow	0.2% in w. or eth.
3.6-5.4	bromocresol green	yellow	blue	0.1% in eth. (20%)
4.0-5.8	2.5-dinitrophenol	colour-less	yellow	0.1% in eth. (70%)
4.4-6.2	methylene red, C.I. 13020	red	yellow	0.1% in eth.
4.8-6.4	chlorphenol red	yellow	purple	0.1% in eth. (20%)
5.2-6.8	bromocresol purple	yellow	purple	0.1% in eth. (20%)
5.4-7.5	4-nitrophenol	colour-less	yellow	0.2% in eth. or 0.08% in w.
5.7-7.4	bromoxylenol blue	yellow	blue	0.1% in eth.

Table 1 (continued)

pH Indicators

Range of visible colour change	Indicator	Colour Change acidic	alkaline	Indicator Solution (eth. = ethanol, w = water)
6.0-7.6	bromothymol blue	yellow	blue	0.1% in eth. (20%)
6.4-8.2	phenol red	yellow	red	0.1% in eth. (20%)
6.6-8.6	3-nitrophenol	colour-less	orange/ yellow	0.08% in w. or 0.3% in eth.
6.8-8.0	neutral red, C.I. 50040	bluish red	orange/ yellow	0.1% in eth. (70%)
7.0-8.8	cresol red	yellow	purple	0.1% in eth.
7.3-8.7	1-naphthol phthalein	brown/ colourl.	greenish blue	0.1% in eth.
7.4-9.0	m-cresol purple	yellow	purple	0.1% in eth. (20%)
8.0-9.6	thymol blue	yellow	blue	0.1% in eth.
8.2-9.8	phenolphthalein	colour-less	reddish violet	0.1% in eth.
9.3-10.5	thymolphthalein	colour-less	blue	0.1% in eth. (50%)
10.0-12.1	alizarin yellow G.G., C.I. 14025	light yellow	brownish yellow	0.1% in w.
11.6-13.0	epsilon blue	orange	violet	0.1% in w.

The cover foil of the pCO_2 indicator may be made from any material impermeable to CO_2 fulfilling the requirements as to the light transparency of the cover foil. Preferably, the material of the cover foil is a thermoplastic material in order to render it possible to provide a dome of the cover foil, below which dome the indicator system containing inner chamber of the pCO_2 indicator is defined.

CLAIMS

1. An apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil.

2. The apparatus according to Claim 1, said indicator system comprising an aqueous solution of a pH-sensitive indicator material generating a visible indication in response to a change of pH.

3. The apparatus according to Claim 2, said indicator material being Bromethymol Blue, and said aqueous solution comprising a buffer, such as $NaHCO_3$.

4. The apparatus according to any of the Claims 1-3, further compising a sponge of an absorbing material, said sponge being concealed within said inner chamber, and said indicator system being soaked in said sponge.

5. The apparatus according to any of the Claims 1-4, further comprising a support foil having a through-going aperture, said support foil being circumferentially joined to said first foil in facial contact therewith through a first side surface of said support foil so as to expose said second foil in said aperture of said support foil.

6. The apparatus according to Claim 5, said support foil being provided with an adhesive layer provided at a side surface of said support foil opposite to said first side surface thereof.

7. The apparatus according to Claim 6, further comprising a release foil covering said adhesive layer and said second foil exposed in said aperture of said support foil.

8. The apparatus according to any of the Claims 1-7, said first foil having a dome, said inner chamber being defined below said dome of said first foil.

9. The apparatus according to any of the Claims 1-8, said first

foil being constituted by a foil of a container or bag containing a material or a sample, the bacteriological activity of which is to be monitored by means of the apparatus.

10. The apparatus according to any of the Claims 7-8, said second foil being constituted by a foil of a container or bag containing a material or a sample, the bacteriological activity of which is to be monitored by means of the apparatus.

11. The apparatus according to Claim 9 or 10, said indicator system being contained within an adhesive layer through which said apparatus is adhered to said foil of said container or bag.

12. The apparatus according to any of the Claims 1-11, further comprising a reference colour coding provided at an outer side surface part of said first foil.

13. The apparatus according to any of the Claims 1-12, said first foil being a multi-layer film comprising at least one layer of nylon and at least one layer of polyethylene.

14. The apparatus according to any of the Claims 1-13, said second foil being a polyethylene foil, said support foil being a PVC foil, and said sponge being a filtre paper sponge, or alternatively a sponge made from woven material or mesh material.

15. An apparatus for indicating the partial pressure of CO_2, comprising:

a foil of a light-transparent, CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2, said foil being folded and sealed so as to define a sealed inner chamber, and said indicator system being enclosed within said inner chamber and being visible through said light-transparent foil.

16. The apparatus according to Claim 15, said foil defining a tubular segment sealed at opposite ends thereof.

17. The apparatus according to Claim 15 or 16, said indicator system comprising an aqueous solution of a pH-sensitive indicator material generating a visible indication in response to a change of pH.

18. The apparatus according to Claim 17, said indicator material being Bromethymol Blue, and said aqueous solution comprising a buffer, such as $NaHCO_3$.

19. The apparatus according to any of the Claims 15-18, further comprising a sponge of an absorbing material, such sponge being conceal-

ed within said inner chamber, and said indicator system being soaked in said sponge.

20. The apparatus according to any of the Claims 15-19, said foil being a polyethylene foil, and said sponge being a filter paper sponge, or alternatively a sponge made from a woven material or mesh material.

21. A method of measuring and indicating bacterial activity within a container or bag having a wall of a gas-permeable material and containing a biological material or sample, comprising the steps of:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil, and

b) arranging said apparatus in facial contact with said wall of said container or bag so as to arrange said second foil in gas-communicating relationship with said wall and said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said wall and through said second foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag.

22. The method according to Claim 21, said apparatus further comprising any of the features of the apparatus according to any of the Claims 2-14.

23. The method according to any of the Claims 21 or 22, said container or bag being a bag containing a thrombocyte suspension.

24. A method of measuring and indicating bacterial activity within a container or bag of a gas-impermeable material containing a biological material or sample, comprising the following steps:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially imperme-

able to gas and water,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil, and

b) arranging said apparatus within said container or bag so as to arrange said second foil in gas-communicating relationship with said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said second foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag, and so as to expose said first foil through a light-transparent section or wall of said container or bag.

25. The method according to Claim 24, said apparatus further comprising any of the features of the apparatus according to any of the Claims 2-11.

26. A method of measuring and indicating bacterial activity within a container or bag of a gas-impermeable material containing a biological material or sample, comprising the steps of:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a first foil of a light-transparent material substantially impermeable to gas and water, constituting at least a wall section of said container or bag,

a second foil of a CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2,

said first and second foils being joined together so as to define an inner chamber between said first and second foils, and said indicator system being enclosed within said inner chamber and being visible through said first foil, and

b) arranging said apparatus so as to arrange said first foil constituting said wall section of said container or bag, and so as to arrange said second foil in gas-communicating relationship with said material or sample contained within said container or bag for causing CO_2

generated within said container or bag by bacterial activity therein to permeate through said second foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag.

27. The method according to Claim 26, said apparatus further comprising any of the features of the apparatus according to any of the Claims 2-14.

28. The method according to any of the Claims 26-27, said container or bag being a bag containing foodstuff.

29. The method of measuring and indicating bacterial activity within a container or bag of a gas-impermeable material containing a biological material or sample, comprising the following steps:

a) providing an apparatus for indicating the partial pressure of CO_2, comprising:

a foil of a light-transparent, CO_2-permeable material, and

an indicator system generating a visible indication in response to exposure to CO_2, said foil being folded and sealed so as to define a sealed inner chamber, and said indicator system being enclosed within said inner chamber and being visible through said light-transparent foil, and

b) arranging said apparatus so as to arrange said foil in gas-communicating relationship with said material or sample contained within said container or bag for causing CO_2 generated within said container or bag by bacterial activity therein to permeate through said foil of said apparatus causing a visible indication of said indicator system representing the bacterial activity within said container or bag, and so as to expose said foil through a light-transparent section or wall of said container or bag.

30. A method according to Claim 29, said apparatus further comprising any of the features of the apparatus according to any of the Claims 16-20.

Fig. 1

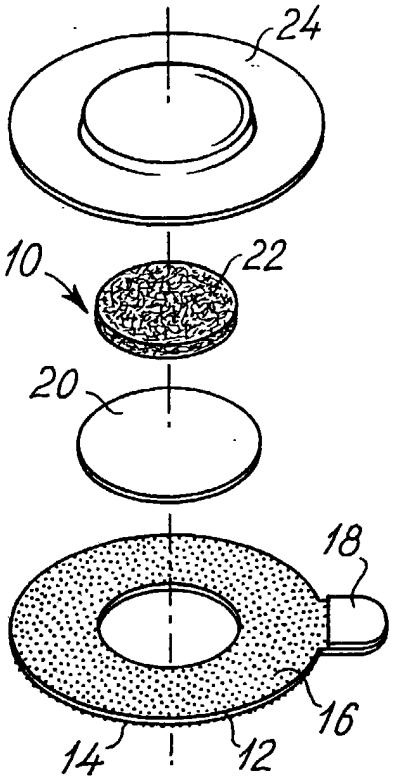


Fig. 2

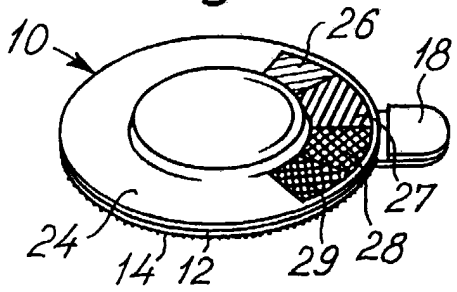


Fig. 4

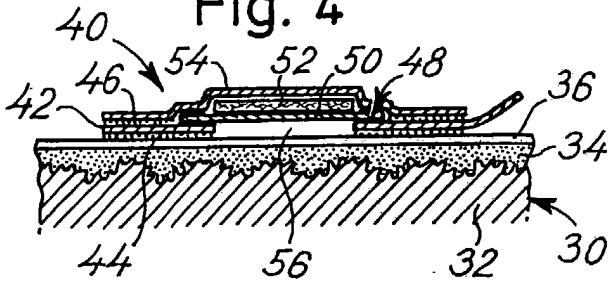


Fig. 5

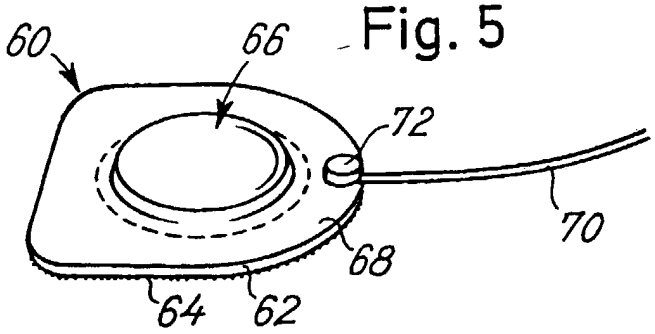
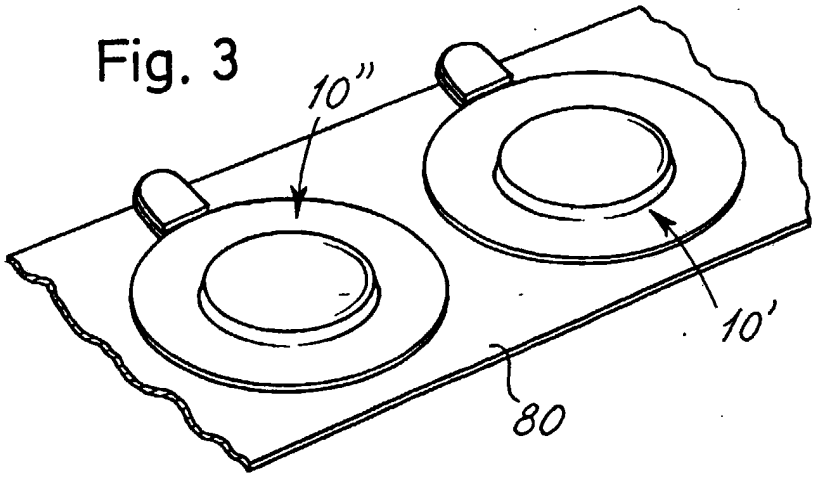


Fig. 3



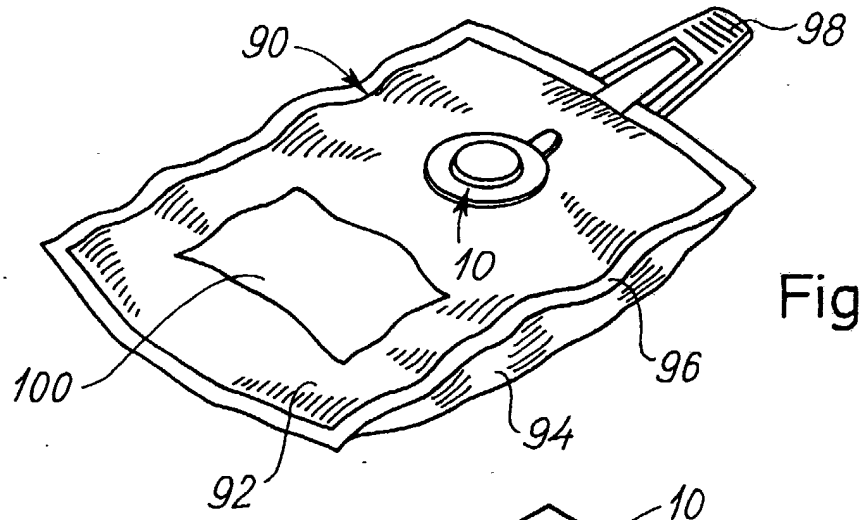


Fig. 6

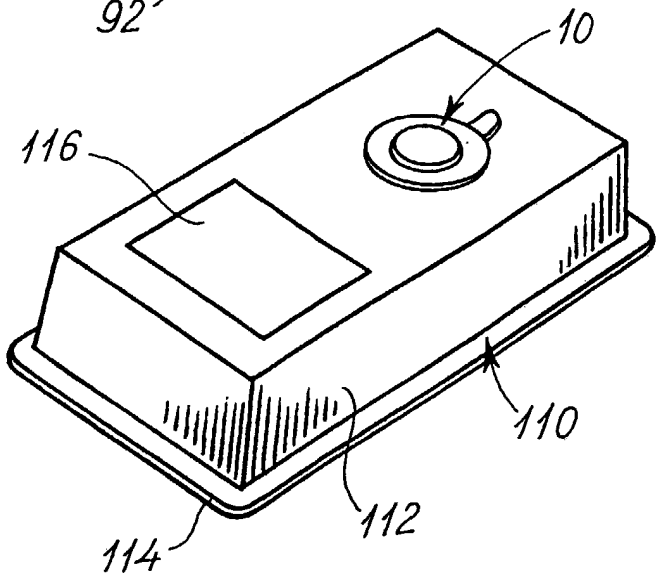


Fig. 7

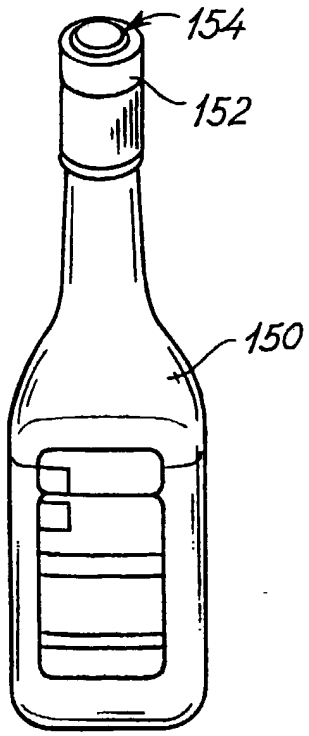


Fig. 8

Fig. 9

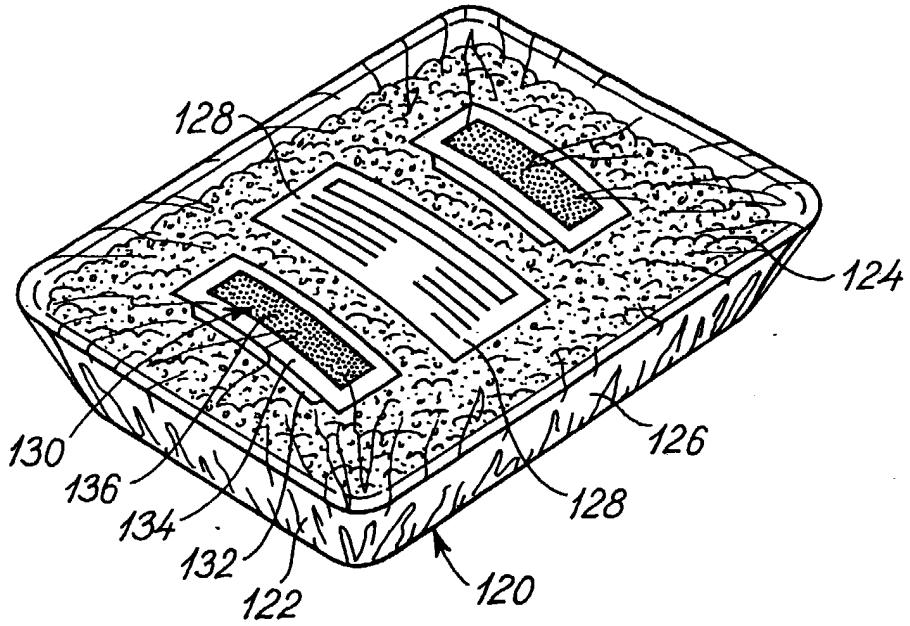

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Fig. 10

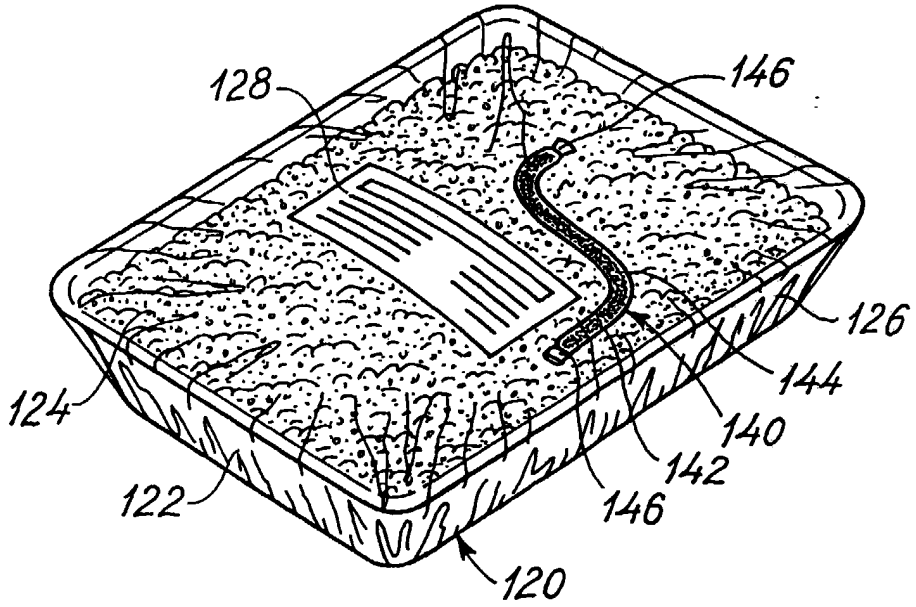
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Fig. 11

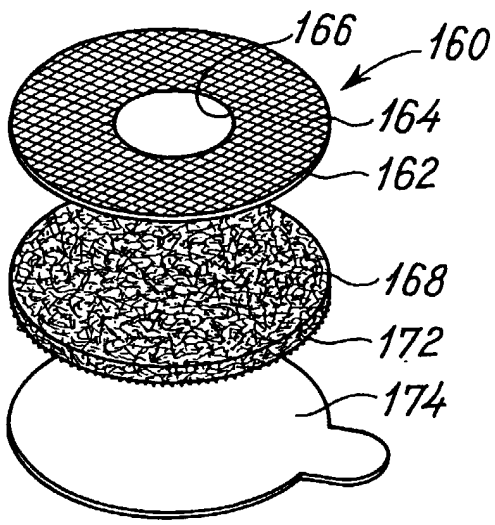


Fig. 12

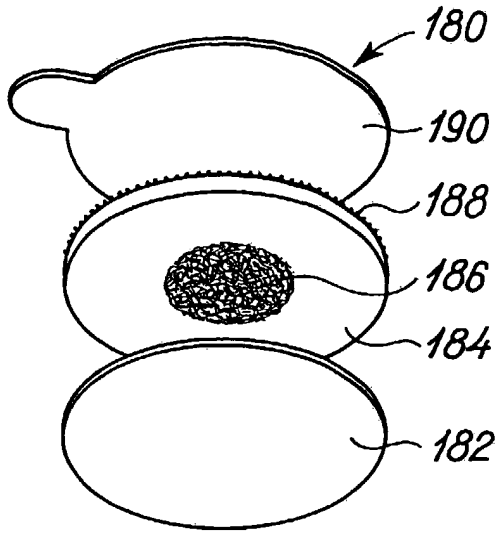


Fig. 13

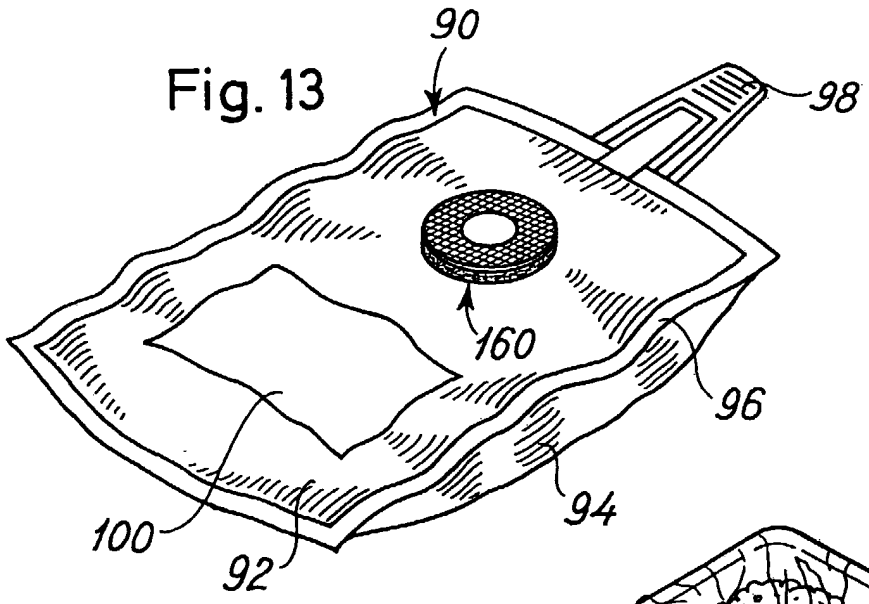
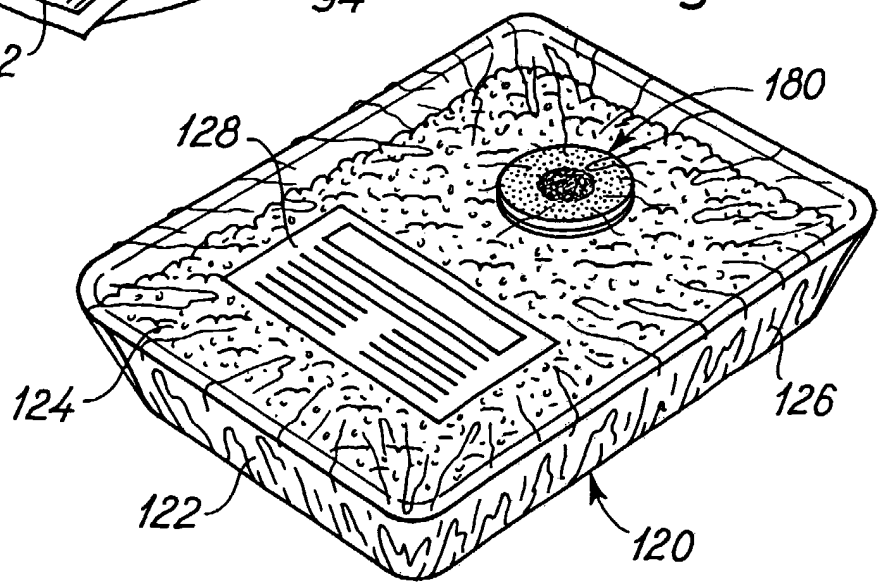


Fig. 14



INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 93/00040

A. CLASSIFICATION OF SUBJECT MATTER

IPC5: G01N 31/22
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC5: G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPIL, WPI, CLAIMS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 4003709 (JOHN C. EATON ET AL.), 18 January 1977 (18.01.77), column 2, line 8 - line 14; column 3, line 3 - line 37, the claims	1-30
A	WO, A1, 8801384 (BARNARD, E. E. ET AL.), 25 February 1988 (25.02.88)	1-30

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 May 1993	01 -06- 1993
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Carolina Palmcrantz Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

31/03/93

International application No.

PCT/DK 93/00040

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 4003709	18/01/77	NONE	
WO-A1- 8801384	25/02/88	AU-A- 4462189	08/03/90
		AU-A- 7681487	18/02/88
		EP-A- 0257916	02/03/88